
17.1 General Background

It has been solidly shown that BD has an unfavourable outcome in a considerable number of patients, in spite of the recent advances in its pharmacological treatment (Fountoulakis et al. 2012; Grunze et al. 2013). Many BD patients eventually suffer from chronic mood symptoms with significant global disability and burden, not only for themselves but also for their family and the society (Murray et al. 2012; Rosa et al. 2010). The overall functional outcome can be captured mainly by two dimensions representing clinical severity and cognitive dysfunction (Reinares et al. 2013). Unfortunately, symptomatic remission does not imply functional recovery which is absent in a significant number of clinically and symptomatically remitted patients (Tohen et al. 2000; Rosa et al. 2011).

Pharmacological treatment often fails to address all the patients' needs and there is a growing need for the development and implementation of effective and affordable interventions, tailored to the individual patient (Catala-Lopez et al. 2013). Early successful treatment, with full recovery if possible, is of prime importance for the long-term outcome. It has been clearly shown that subsyndromal symptoms together with psychosocial stress at baseline are factors predicting earlier relapse (De et al. 2012). Longitudinal studies show that poor adherence is also predictive of a poorer long-term outcome (Berk et al. 2010).

There are several specific adjunctive psychotherapies which have been developed with the aim to fill the above gaps and eventually to improve the illness outcome (Geddes and Miklowitz 2013). It is still unclear which psychotherapies truly work and which patients are eligible. The time of intervention is also an open question (Scott et al. 2006; Miller et al. 2004; Meyer and Hautzinger 2012; de Barros et al. 2013; Gomes et al. 2011; Reinares et al. 2014; Fountoulakis and Siamouli 2009a). Acute depression and the maintenance phase but not acute mania are at the centre of research.

Concerning the quality of the data available, the studies in BD patients suffer from the same limitations and methodological problems all psychotherapy

trials do. There is no universally accepted standardized method to conduct this kind of studies and blindness and the nature of the control intervention are unresolved limitations.

17.2 Specific Psychotherapies and Psychosocial Interventions

17.2.1 Cognitive-Behavioural Therapy (CBT)

CBT for BD includes education about BD as a diathesis–stress illness, enhances the cognitive-behavioural skills to cope with prodromes, stresses the importance of routine and sleep, deals with cognitive and behavioural barriers to treatment adherence and guides the patient towards the identification of triggering factors and the dealing with long-term vulnerabilities. It also challenges dysfunctional thoughts and underlying maladaptive assumptions.

There are a small number of studies which investigate the usefulness of CBT in BD. All of them utilize CBT as adjunct treatment on pharmacotherapy and all have inadequate placebo conditions as control.

The first study on CBT in bipolar depression included 103 BD-I patients and randomized them to 14 sessions of CBT or a control group which however did not include any placebo condition. During a 12-month period, fewer patients in the CBT group relapsed in comparison to controls (44 % vs. 75 %). Also, patients in the control group had shorter duration in an episode, less admissions and mood symptoms and higher social functioning (Lam et al. 2003). However, the report of an extension (18-month follow-up) reported no effect of CBT on the relapse rate (Lam et al. 2005b).

Another study on 52 BD patients confirmed this loss of efficacy during the follow-up in a study which compared CBT plus additional emotive techniques vs. treatment as usual (TAU) (Ball et al. 2006). The comparison of CBT plus psychoeducation vs. TAU in 40 BD patients reported a beneficial effect even after 5 years in terms of symptoms and social–occupational functioning, but rate of recurrences and time to recurrence were not reported (Gonzalez-Isasi et al. 2012). CBT plus psychoeducation has been proven superior to psychoeducation alone in a study of 79 BD patients (52 BD-I and 27 BD-II). In that study, the combined treatment group had 50 % fewer depressed days per month, while at the same time the psychoeducation-alone group had more antidepressant use (Zaretsky et al. 2008). Similar results were reported from a study in 41 BD patients randomized to CBT vs. TAU. The results suggested an improvement in symptoms, frequency and duration of episodes (Costa et al. 2011).

A study which compared CBT vs. TAU in 253 BD patients reported that after 18 months more than half of the patients had a recurrence and there was no difference between groups. The post hoc analysis demonstrated that CBT was significantly more effective than TAU in those patients with fewer than 12 previous episodes, but less effective in those with more episodes (Scott et al. 2006). Similarly,

no differences were reported at 12 months concerning the number of episodes and time to relapse by another study in 50 BD patients in remission which compared CBT vs. TAU (Gomes et al. 2011). Finally a 2-year study on 76 BD patients which were randomized to receive 20 sessions of CBT vs. support therapy reported negative findings concerning the relapse rate (Meyer and Hautzinger 2012).

Overall, the data so far give limited support for the usefulness of CBT during the acute phase of bipolar depression but definitely not for the maintenance for which booster sessions might be necessary and further research on the issue is needed. Probably patients at earlier stages of the illness might benefit more by this specific intervention, while those patients with a high chronicity and severity may have a worse response to the treatment. Unfortunately the type of patients which are more likely to benefit from CBT constitutes a minority in usual clinical practice.

17.3 Psychoeducation

Psychoeducation for BD includes training of patients regarding the overall awareness of the disorder, the treatment adherence, the avoiding of substance abuse as well as the early detection of new episodes. It also focuses on regular habits and stress management.

One of the first studies concerning the teaching of patients to recognize and identify the components of their disease and especially early symptoms of relapse and recurrence and to seek professional help as early as possible followed 69 patients for 18 months and compared psychoeducation to TAU and reported significant prolongation of the time to first manic relapse ($p=0.008$) and significant reductions in the number of manic relapses over 18 months (30 % vs. 52 %; $p=0.013$). The experimental treatment had no effect on time to first relapse or number of relapses with depression, but it significantly improved overall social functioning. It is important to note that the psychoeducation method included a limited number of sessions (7–12) (Perry et al. 1999).

The efficacy of adjunctive group psychoeducation was tested by the Barcelona group. Their trial included 120 euthymic BD patients who were randomly assigned to 21 sessions of group psychoeducation vs. non-specific group meetings. In this specific trial, psychoeducation involved improvement of illness awareness, detection of prodromes, adherence enhancement, substance use avoidance, encouragement of regular habits and stress management. The study included a follow-up with a duration of 2 years and reported that psychoeducation exerted a beneficial effect on the rate of and the time to recurrence as well as concerning hospitalizations per patient. This beneficial effect was high and was not reduced after 5 years (any episode 0.79 vs. 0.87; mania 0.40 vs. 0.57; hypomania 0.27 vs. 0.42 and mixed episodes 0.34 vs. 0.61), except for depressive episodes (0.91 vs. 0.80). Subjects in the psychoeducation group were acutely ill much less time (Colom et al. 2003, 2009).

Enhanced relapse prevention alone does not seem to work since another study with a different design reported that only occupational functioning but not time to recurrence improved with an intervention consisting of training community mental

health teams to deliver enhanced relapse prevention (Lobban et al. 2010). Also a study with a 12-month follow-up and with a similar design to the first study of the Barcelona group but with 16 sessions found no differences between groups in mood symptoms, psychosocial functioning and quality of life, except for a subjectively perceived overall clinical improvement by subjects who received psychoeducation. The authors suggested that characteristics of the sample could explain this discrepancy, as patients with a more advanced stage of disease might have a worse response to psychoeducation (de Barros et al. 2013). In accord with the above, a post hoc analysis of the original Barcelona data revealed that patients with more than seven episodes did not show significant improvement with group psychoeducation in time to recurrence, and those with more than 14 episodes did not benefit from the treatment in terms of time spent ill (Colom et al. 2010).

The cost for the treatment of BD might be reduced with group psychoeducation (Scott et al. 2009). One trial in 204 BD patients applied 20 sessions of CBT or 6 sessions of group psychoeducation and found that overall the outcome was similar in the two groups in terms of reduction of symptoms and likelihood of relapse, but psychoeducation was associated with a decrease of costs (\$180 per subject vs. \$1,200 per subject for CBT) (Parikh et al. 2012) Currently there are some proposals of online psychoeducation programmes, but results are still inconclusive or pending (Smith et al. 2011; Proudfoot et al. 2012).

More complex multimodal approaches and multicomponent care packages have been developed and usually psychoeducation is a core element. One of these packages also included CBT and elements of dialectical behaviour therapy and social rhythms and has shown a beneficial effect after 1-year follow-up in comparison to TAU (Castle et al. 2010). The beneficial effect seems to be present concerning manic but not depressive episodes (Bauer et al. 2006; Simon et al. 2006), while a benefit on social role function and quality of life seems also to be present (Bauer et al. 2006).

Overall, the data so far suggest that interventions of a 6-month group psychoeducation seem to exert a long-lasting prophylactic effect, but this is probably restricted to manic episodes and to patients at the earlier stages of the disease who have achieved remission before the intervention has started. Although the mechanism of action of psychoeducation remains unknown, it is highly likely that the beneficial effect is mediated by the enhancement of treatment adherence, the promoting of lifestyle regularity and healthy habits and the teaching of early detection of prodromal signs.

17.4 Interpersonal and Social Rhythm Therapy (IPSRT)

IPSRT is based on the hypothesis that stressful life events and unstable or disrupted daily routines can lead to circadian rhythm instability and, in vulnerable individuals, to affective episodes (Reinares et al. 2014). It includes the management of affective symptoms through improvement of adherence to medication and stabilizing social rhythms and the resolution of interpersonal problems (unresolved grief, social

role transitions, interpersonal role disputes, interpersonal deficits, grief for the lost healthy self).

There are only limited data concerning its usefulness. The first study included 175 acutely ill BD patients and followed them for 2 years. The trial involved four treatment groups depending on the combination of treatment and phase, that is, IPSRT vs. intensive clinical management during the acute and the maintenance phase. Overall, the data suggested there was no difference between IPSRT and intensive clinical management in terms of time to remission and in the proportion of patients achieving remission (70 % vs. 72 %). A positive finding was that those patients who received IPSRT during the acute treatment phase survived longer without an episode and showed higher regularity of social rhythms (Frank et al. 2005). Regarding psychosocial functioning, the results suggested that especially women who initially received IPSRT showed faster improvement in occupational functioning, but again there were no differences between groups at the end of the follow-up (Frank et al. 2008). More recently, a 12-week study in which unmedicated depressed BD-II patients were randomized to IPSRT ($N=14$) vs. treatment with quetiapine (up to 300 mg/day; $N=11$) showed that both groups experienced significant reduction in symptoms over time, but there were no group-by-time interactions. Response and dropout rates were similar (Swartz et al. 2012).

Overall, there are no convincing data on the usefulness of IPSRT during the maintenance phase of BD; however, there are some data suggesting that if applied early and particularly already during the acute phase, it might prolong the time to relapse.

17.5 Family Intervention

Family intervention for BD includes psychoeducation, communication enhancement and problem-solving skills training, as well as support and self-care training for caregivers. Family intervention targets the whole family and not only the patient.

There are significantly more studies on the possible usefulness of family intervention in BD patients. The importance of involving the whole family in the treatment intervention was highlighted in a study of 81 BD patients and 33 family dyads, which reported that the odds ratio for hospitalization at 1-year follow-up was related with high perceived criticism (by the patients from their relatives), poor adherence and the relatives' lack of knowledge concerning BD (OR 3.3; 95 % CI: 1.3–8.6) (Scott et al. 2012).

Several studies support the use of adjunctive family-focused treatment. One intervention design consists of 21 one-hour sessions which combine psychoeducation, communication skills training and problem-solving training. The sessions take place at home and include both the patient and his/her family during the post-episode period. The treatment has shown its efficacy vs. crisis management in 101 BD patients in reducing relapses (35 % vs. 54 %) and increasing time to relapse (53 vs. 73 weeks, respectively) (Miklowitz et al. 2000, 2003) and to reduce hospitalization risk compared with individual treatment (12 % vs. 60 %) (Rea et al. 2003).

The benefits extended to a 2-year follow-up and were particularly useful for depressive symptoms, in families with high expressed emotion and for the improvement of medication adherence (Miklowitz et al. 2003). Another format of intervention included 12 sessions of group psychoeducation for the patients and their families, and in comparison to TAU in 58 BD patients, it was reported to have a beneficial effect in the prevention of relapses, the decreasing of manic symptoms and the improvement of medication adherence (D'Souza et al. 2010).

Improvement in a variety of peripheral problems that accompany BD has been reported with several types of family intervention. Adjunctive psychoeducational marital intervention in acutely ill patients was reported to have a beneficial effect concerning medication adherence and global functioning but not for symptoms (Clarkin et al. 1998). It is almost certain that neither adjunctive family therapy nor adjunctive multifamily group therapy improves the recovery rate from acute bipolar episodes when compared with pharmacotherapy alone (Miller et al. 2004); however, it seems that these interventions could be beneficial for patients from families with high levels of impairment and could result in a reduction of both the number of depressive episodes and the time spent in depression (Cohen $d=0.7-1.0$) (Miller et al. 2008). In this frame, in those patients who recovered from the intake episode, multifamily group therapy was associated with the lowest hospitalization risk (Solomon et al. 2008).

A 15-month RCT showed the benefits in the prevention of recurrences of 12 group sessions of psychoeducation with a 90-min duration, delivered to caregivers of euthymic BD patients. This intervention was reported to have both reduced the risk of recurrence in comparison to a control group (42 % vs. 66 %; NNT: 4.1 with 95 % CI: 2.4–19.1) and also to have delayed recurrence (Reinares et al. 2008). It seemed that this intervention was particularly efficacious in the prevention of hypomanic/manic episodes and also in the reduction of the overall family burden (Reinares et al. 2004). It seems reasonable and also it is supported by research that carer-focused interventions improve the knowledge of the illness (van Gent and Zwart 1991), reduce burden (Madigan et al. 2012) and also reduce the general and mental health risk of caregivers (Perlick et al. 2010).

Overall, the literature supports the idea that interventions which focus on families and caregivers exert a beneficial impact especially on family members. The effect includes issues ranging from subjective well-being to general health. The effect on the patients themselves is controversial, but it is almost certain that there is a beneficial effect on issues like treatment adherence.

17.6 Intensive Psychosocial Intervention

'Intensive' psychotherapy is another option, but it is of unknown general efficacy. In BD patients it has been tested on 293 acutely depressive outpatients in multi-site study. These patients were randomized to 3 sessions of psychoeducation or up to 30 sessions of intensive psychotherapy (family-focused therapy, IPSRT or CBT). The methodology suffered from a number of drawbacks and the two groups were not

well matched. The intensive psychotherapy group showed higher recovery rates, shorter times to recovery and greater likelihood of being clinically well in comparison to patients on the short intervention (Miklowitz et al. 2007b). The functional outcome was also reported to be better after 1 year (Miklowitz et al. 2007a).

17.7 Cognitive Remediation and Functional Remediation

As mentioned in the relevant chapter of the current book, BD patients suffer from severe and persistent neurocognitive dysfunction. There are already developed psychotherapeutic and other non-pharmacological methods to address this problem in patients with schizophrenia, but the experience from their application is rather disappointing in spite of favourable meta-analytic reports (Anaya et al. 2012).

Functional remediation tailored for the needs of BD patients includes education on neurocognitive deficits, communication, autonomy and stress management.

So far a similar picture seems to be in place concerning BD as well, with the limited research data that exist, failing to provide solid support to this kind of intervention.

One uncontrolled study in 15 BD patients applied a type of cognitive rehabilitation intervention and focused on mood monitoring and residual depressive symptoms, organization, planning and time management, attention and memory. An improvement of residual depressive symptoms, executive functions and general functioning was described. Patients with greater neurocognitive impairment had less benefit from the intervention (Deckersbach et al. 2010). The combination of neurocognitive techniques with psychoeducation and problem-solving within an ecological framework was tested in a multicentre trial in 239 euthymic BD patients with a moderate–severe degree of functional impairment ($N=77$) vs. psychoeducation ($N=82$) and vs. TAU ($N=80$). At endpoint the combined programme was superior to TAU but not to psychoeducation alone (Martinez-Aran et al. 2011; Torrent et al. 2013). A small study in 37 BD and schizoaffective patients tested Social Cognition and Interaction Training (SCIT) as adjunctive to TAU ($N=21$) vs. TAU alone ($N=16$). There was no difference between groups concerning social functioning, but there was a superiority of the combination group in the improvement of emotion perception, theory of mind, hostile attribution bias and depressive symptoms (Lahera et al. 2013).

17.8 Mindfulness-Based Interventions

The basic concept of mindfulness-based training is to enhance the ability to keep one's attention on purpose in the present moment and non-judgmentally. For BD patients it includes education about the illness and relapse prevention, combination of cognitive therapy and training in mindfulness meditation to increase the awareness of the patterns of thoughts, feelings and bodily sensations and the development of a different way (non-judgmentally) of relating to thoughts, feelings and bodily

sensations. It also promotes the ability of the patients to choose the most skilful response to thoughts, feelings or situations.

The first study concerning the application of mindfulness-based cognitive therapy (MBCT) in BD tested it in comparison to waiting list and included only 8 patients in each group. The results suggested a beneficial effect with a reduction in anxiety and depressive symptoms (Williams et al. 2008).

Another study included 23 BD patients and 10 healthy controls and also utilized brain fMRI. Sixteen of these patients were tested before and after an 8-week MBCT intervention, and seven were wait-listed for training and tested at the same intervals. The results were compared with those of 10 healthy controls. Following MBCT, there were significant improvements in BD patients concerning mindfulness, anxiety and emotion regulation, working memory, spatial memory and verbal fluency compared to the bipolar wait-list group (Ives-Deliperi et al. 2013).

The biggest study so far concerning MBCT included 95 BD patients and tested MBCT as adjunctive to TAU ($N=48$) vs. TAU alone ($N=47$) and followed the patients for 12 months. The results showed no difference between treatment groups in terms of relapse and recurrent rates of any mood episodes. There was some beneficial effect of MBCT on anxiety symptoms (Perich et al. 2013a, b).

Recently, the focus has expanded to analyse the impact of MBCT on brain activity and cognitive functioning in BD, but the findings are difficult to interpret (Howells et al. 2012; Stange et al. 2011; Ives-Deliperi et al. 2013).

A study which applied dialectical behaviour therapy in which mindfulness represented a large component also reported some positive outcomes (Van et al. 2013).

Overall, the data do not support a beneficial effect of MBCT on the core issues of BD but also suggest that MBCT could be useful in the reduction of anxiety in BD patients. So far there are no data supporting its efficacy in the prevention of recurrences.

Conclusions

Reviewing the data on the usefulness of psychosocial intervention in BD is rather disappointing. It seems that only psychoeducation is efficacious for the relapse prevention of mood episodes but only in a selected subgroup of patients at an early stage of the disease who have very good if not complete remission of the acute episode. CBT and IPSRT could have some beneficial effect during the acute phase, but more data are needed. Mindfulness interventions could only decrease anxiety, while interventions to improve neurocognition seem to be rather ineffective. Family intervention seems to have benefits mainly for caregivers, but it is uncertain whether they have an effect on patient outcomes. A summary of the specific areas of efficacy for each of the above-mentioned interventions is shown in Table 17.1.

The mechanisms responsible for the efficacy of the psychosocial treatments are unknown and poorly studied. Opinions suggest that the effect could be mediated through enhancement of treatment adherence (Colom et al. 2005); improving the lifestyle and especially biological rhythms, food intake and social zeitgebers (Frank et al. 2005); the changing of dysfunctional attitudes

Table 17.1 Specific psychosocial interventions and their targeted therapeutic effect in BD

Intervention	Efficacy						
	Relapse/recurrence	Manic symptoms	Depressive symptoms	Anxiety	Neurocognition	Overall functioning	
CBT	No	–	Yes	–	–	–	
Psychoeducation	Yes	No	No	–	–	Yes	
IPSRT	E	E	E	–	–	–	
Family intervention	No	No	No	–	–	No	
Intensive psychosocial intervention	–	–	–	–	–	–	
Cognitive remediation	No	No	No	–	No	No	
Mindfulness-based interventions	No	No	No	Yes	–	–	

(Ball et al. 2006); but also through the improvement of family interactions (Simoneau et al. 1999a, b). The enhanced ability for the early identification of signs of relapse may play an important role too (Perry et al. 1999).

As in any trial concerning any psychological intervention, the methodological issues hampering research are cardinal. The blindness problem together with the impossible task to have a valid placebo group limits the value of the data. Because of these methodological drawbacks, often small studies of this kind have an unexpectedly high effect size, while at the same time there is a lack of replication of the same treatment by different research groups under the same conditions. Psychosocial interventions suffer from an additional drawback themselves. The training of the therapist and the setting itself might play an important role and it is quite different to apply the same intervention in specialized centres than in real-world settings in the everyday clinical practice. Furthermore, the gathering of the data is far from systematic; adverse events are not routinely registered, outcomes are not hierarchically stated a priori and too many post hoc analyses are published without being stated as such.

The best timing for the implementation of psychological interventions is still uncertain, but it seems that they function better in subjects which are at an early stage of the disease and who were euthymic when recruited (Scott et al. 2007; Miller et al. 2004). It is highly possible that a higher number of previous episodes (Colom et al. 2010; Scott et al. 2006) as well as a higher psychiatric morbidity and more severe functional impairment (Reinares et al. 2010) might reduce treatment response although the data are not conclusive (Lam et al. 2009). In addition, it has been suggested that in the early phases, the intervention should be simpler, with a focus on neuroprotective strategies (Kapczinski et al. 2009). At later stages, the emphasis could focus more on rehabilitative interventions dealing with the specific disabilities of the patients (Berk et al. 2007).

IPSRT and CBT might be also efficacious during the acute episodes, but this is far from clear (Miklowitz et al. 2007b; Frank et al. 2005; Scott et al. 2006). Specific characteristics of the family environment have also been shown to influence the response to treatment (Miller et al. 2008; Miklowitz et al. 2009). Probably there were subpopulations who will especially benefit from these treatments (Scott et al. 2006; Miller et al. 2008), but these assumptions are based on post hoc analyses alone.

It should be mentioned that most of research concerns pure and classic BD-I patients although there are some rare data concerning special populations like BD-II (Colom et al. 2009; Swartz et al. 2012), schizoaffective disorder (Vieta 2010; Murru et al. 2012), patients with high suicide risk (Fountoulakis et al. 2009; Fountoulakis and Siamouli 2009b; Williams et al. 2008) and patients with comorbid substance abuse (Weiss et al. 2007, 2009).

The literature includes reports which suggest that the benefits of psychosocial interventions if achieved can last for up to 5 years (Gonzalez-Isasi et al. 2010; Colom et al. 2009) although some patients might need booster sessions (Lam et al. 2005a; Ball et al. 2006). The complete range of the effect these interventions have is still uncharted. It is reasonable to expect a beneficial effect

in a number of problems, including suicidality, but research data on these issues are virtually non-existent (Fountoulakis et al. 2009; Fountoulakis and Siamouli 2009b).

Overall, there are some data in the literature supporting the notion that adjunctive specific psychological treatments can improve specific illness outcomes. It seems reasonable that any such intervention should be applied as early as possible and should always be tailored to the specific needs of the patient in the context of personalized patient care, since it is accepted that both the patients and their relatives have different needs and problems depending on the stage of the illness.

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